

WHAT IS CLAIMED:

1. A method for identifying an analyte which directly or indirectly modulates activity of a glucocorticoid receptor in the brain of an animal, which comprises:

5 (a) administering a glucocorticoid to a first animal and measuring an amount of tryptophan hydroxylase (TPH2) in the brain of the first animal; and

(b) administering the glucocorticoid and the analyte to a second animal and measuring the amount of the TPH2 in the brain of the second animal wherein a change in the amount of the TPH2 in the brain of the second animal relative to the amount of the TPH2 in the first animal indicates that the
10 analyte modulates the activity of the glucocorticoid receptor in the brain of the animal.

2. The method of Claim 1 wherein the TPH2 is TPH2 mRNA and the TPH2 mRNA is measured by reverse transcription-polymerase chain reaction (RT-PCR).

15 3. The method of Claim 2 wherein the RT-PCR is a real-time RT-PCR which uses an oligonucleotide probe comprising a nucleotide sequence complementary to a nucleotide sequence comprising the TPH2 mRNA.

20 4. The method of Claim 1 wherein the TPH2 is TPH2 RNA and the TPH2 mRNA is measured by *in situ* hybridization which uses an oligonucleotide probe comprising a nucleotide sequence complementary to a nucleotide sequence comprising the TPH2 mRNA.

5. A method for determining the effect of an analyte on an amount of tryptophan hydroxylase isoform 2 (TPH2) in the brain of an animal, which comprises:

25 (a) administering the analyte to the animal; and

(b) measuring the amount of the TPH2 in the brain of the animal wherein a change in the amount of the TPH2 in the brain of the animal compared to the amount of the TPH2 in the brain of the animal without the analyte indicates that the analyte has an effect on the amount of the TPH2 in the
30 brain of the animal.

6. The method of Claim 5 wherein the TPH2 is TPH2 mRNA and the TPH2 mRNA is measured by reverse transcription-polymerase chain reaction (RT-PCR).

7. The method of Claim 6 wherein the RT-PCR is a real-time RT-PCR which uses an oligonucleotide probe comprising a nucleotide sequence complementary to a nucleotide sequence comprising the TPH2 mRNA.

5 8. The method of Claim 5 wherein the TPH2 is TPH2 RNA and the TPH2 mRNA is measured by *in situ* hybridization which uses an oligonucleotide probe comprising a nucleotide sequence complementary to a nucleotide sequence comprising the TPH2 mRNA.

10 9. A method for determining whether an analyte directly or indirectly affects the amount of tryptophan hydroxylase isoform 2 (TPH2) in the brain of an animal which has chronically elevated glucocorticoid levels, which comprises:

(a) providing an animal which has the chronically elevated glucocorticoid levels;
(b) administering the analyte to the animal which has the chronically elevated glucocorticoid levels; and

15 (c) measuring the amount of the TPH2 in the brain of the animal wherein an increase in the amount of the TPH2 in the brain of the animal compared to the amount of the TPH2 in the brain of the animal without the analyte indicates that the analyte has an effect on the amount of the TPH2 in the animal which has the chronically elevated glucocorticoid levels.

20 10. The method of Claim 9 wherein the TPH2 is TPH2 mRNA and the TPH2 mRNA is measured by reverse transcription-polymerase chain reaction (RT-PCR).

25 11. The method of Claim 10 wherein the RT-PCR is a real-time RT-PCR which uses an oligonucleotide probe comprising a nucleotide sequence complementary to a nucleotide sequence comprising the TPH2 mRNA.

30 12. The method of Claim 9 wherein the TPH2 is TPH2 RNA and the TPH2 mRNA is measured by *in situ* hybridization which uses an oligonucleotide probe comprising a nucleotide sequence complementary to a nucleotide sequence comprising the TPH2 mRNA.

13. A method for identifying an analyte which directly or indirectly suppresses glucocorticoid levels in an animal which has chronically elevated glucocorticoid levels, which comprises:
(a) providing an animal having the chronically elevated glucocorticoid levels;
(b) administering the analyte to the animal with the chronically elevated glucocorticoid levels; and

35

(c) measuring an amount of tryptophan hydroxylase isoform 2 (TPH2) in the brain of the animal wherein an increase in the amount of the TPH2 in the brain of the animal compared to the amount of the TPH2 in the brain of the animal without the analyte indicates that the analyte suppresses the glucocorticoid levels in the animal which has the chronically elevated glucocorticoid levels.

5

14. The method of Claim 13 wherein the TPH2 is TPH2 mRNA and the TPH2 mRNA is measured by reverse transcription-polymerase chain reaction (RT-PCR).

15. The method of Claim 14 wherein the RT-PCR is a real-time RT-PCR which uses an oligonucleotide probe comprising a nucleotide sequence complementary to a nucleotide sequence comprising the TPH2 mRNA.

16. The method of Claim 13 wherein the TPH2 is TPH2 RNA and the TPH2 mRNA is measured by *in situ* hybridization which uses an oligonucleotide probe comprising a nucleotide sequence complementary to a nucleotide sequence comprising the TPH2 mRNA.

17. A method for determining whether an analyte is a full glucocorticoid agonist or antagonist or partial glucocorticoid agonist in the brain of an animal, which comprises:

- (a) administering the analyte to a first animal and measuring an amount of tryptophan hydroxylase isoform 2 (TPH2) in the brain of the first animal;
- (b) administering a glucocorticoid to a second animal and measuring an amount of the TPH2 in the brain of the second animal;
- (c) administering the glucocorticoid and the analyte to a third animal and measuring an amount of the TPH2 in the brain of the third animal; and
- (d) comparing the amount of the TPH2 in the brains of the first, second, and third animals wherein (1) a decrease in the TPH2 in the brain of the first animal and a decrease in the TPH2 in the brain of the second animal which is not greater than the decrease in the TPH2 in the brain of the third animal indicates that the analyte is a full agonist, (2) an increase in TPH2 in the brain of the first animal and an increase in the TPH2 in the brain of the third animal compared to the TPH2 in the brain of the second animal indicates that the analyte is a full antagonist, and (3) a decrease in the TPH2 in the brain of the first animal and a decrease in the TPH2 in the brain of the second animal which is greater than the decrease in the TPH2 in the brain of the third animal indicates that the analyte is a partial agonist.

18. The method of Claim 17 wherein the TPH2 is TPH2 mRNA and the TPH2 mRNA is measured by reverse transcription-polymerase chain reaction (RT-PCR).

19. The method of Claim 18 wherein the RT-PCR is a real-time RT-PCR which uses an oligonucleotide probe comprising a nucleotide sequence complementary to a nucleotide sequence comprising the TPH2 mRNA.

5

20. The method of Claim 17 wherein the TPH2 is TPH2 RNA and the TPH2 mRNA is measured by *in situ* hybridization which uses an oligonucleotide probe comprising a nucleotide sequence complementary to a nucleotide sequence comprising the TPH2 mRNA.

10

21. A method for identifying an analyte that directly or indirectly suppresses glucocorticoid disruption of central serotonergic neurotransmission in the brain of an animal, which comprises:

(a) administering a glucocorticoid to a first animal and measuring an amount of tryptophan hydroxylase (TPH2) in the brain of the first animal; and

15

(b) administering the glucocorticoid and the analyte to a second animal and measuring an amount of the TPH2 in the brain of the second animal wherein a change in the amount of the TPH2 in the brain of the second animal relative to the amount of the TPH2 in the first animal indicates that the analyte suppresses the glucocorticoid disruption of the central serotonergic neurotransmission in the brain of the animal.

20

22. The method of Claim 21 wherein the TPH2 is TPH2 mRNA and the TPH2 mRNA is measured by reverse transcription-polymerase chain reaction (RT-PCR).

25

23. The method of Claim 23 wherein the RT-PCR is a real-time RT-PCR which uses an oligonucleotide probe comprising a nucleotide sequence complementary to a nucleotide sequence comprising the TPH2 mRNA.

30

24. The method of Claim 21 wherein the TPH2 is TPH2 RNA and the TPH2 mRNA is measured by *in situ* hybridization which uses an oligonucleotide probe comprising a nucleotide sequence complementary to a nucleotide sequence comprising the TPH2 mRNA.

25. A kit for identifying an analyte which suppresses glucocorticoid disruption of central serotonergic neurotransmission in the brain of an animal, which comprises:

(a) at least one oligonucleotide probe which has a nucleotide sequence complementary to a nucleotide sequence comprising an mRNA encoding tryptophan hydroxylase isoform 2 (TPH2); and

(b) instructions for using the kit.

5

26. The kit of claim 25 wherein the kit further includes a primer pair which flank the region of the nucleotide sequence comprising the mRNA which is complementary to the oligonucleotide probe.

10

27. The kit of Claim 25 or 26 wherein the kit further includes one or more components selected from the group consisting of a reverse transcriptase buffer, a reverse transcriptase enzyme, a polymerase chain reaction (PCR) buffer, dNTPs, and a thermostable DNA polymerase.

15

28. The kit of Claim 25 wherein the kit further includes one or more reagents for *in situ* hybridization.